IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:	)	Examiner: Angell, Jon E.
Avi J. ASHKENAZI, et al.	)	Art Unit: 1635
Application Serial No. 09/978,564	)	Confirmation No. 5282
Filed: October 16, 2001	)	Attorney's Docket No. 39780-2630 P1C25
For: **SECRETED AND TRANSMEMBRANE POLYPEPTIDES AND NUCLEIC ACIDS ENCODING THE SAME**	)	**Customer No. 35489**

DECLARATION OF DR. LUC DESNOYERS, DR. ELLEN FILVAROFF, DR. WEI-QIANG GAO, DR. AUDREY GODDARD, DR. PAUL J. GODOWSKI, DR. AUSTIN GURNEY and DR. WILLIAM I. WOOD, UNDER 37 C.F.R. §1.131

MAIL STOP AF
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

Dear Sir:

We, Luc Desnoyers, Ph.D., Ellen Filvaroff, Ph.D., Wei-Qiang Gao, Ph.D., Audrey Goddard, Ph.D., Paul J. Godowski, Ph.D., Austin Gurney, Ph.D. and William I. Wood, Ph.D. declare and say as follows:

1. We are the inventors of the above-identified application. We have read and understood the claims pending in this application, and are aware that the claims stand rejected as allegedly being unpatentable over Holtzman *et al.*, U.S. 2002/0055139, published May 9, 2002 with priority to May 14, 1999. Holtzman *et al.* teach a polypeptide (human A236 protein) that is 100% identical to SEQ ID NO:59.

2. The polypeptide designated as PRO363 (SEQ ID NO:59), antibodies to which are claimed in the above-identified application, was sequenced, cloned and identified as having homology to the cell surface protein HCAR in the United States prior to May 14,1999.

3. U.S. Provisional Application No. 60/078,910, filed on March 20, 1998, discloses sequences designated as SEQ ID NO:1 and SEQ ID NO:3. The native sequence polypeptide of

SEQ ID NO:3 is identical to SEQ ID NO:59 of the above-identified application, while SEQ ID NO:1 is identical to SEQ ID NO:58 of the above-identified application. A copy of U.S. Provisional Application No. 60/078,910 is enclosed as **Exhibit A**.

4. U.S. Provisional Application No. 60/078,910, filed on March 20, 1998 further discloses that SEQ ID NO:3, corresponding to SEQ ID NO:59 of the above-identified application, has homology to the cell surface protein HCAR.

5. At the time the present invention was made, one of the inventors, Wei-Quiang Gao, Ph.D., was responsible for overseeing the testing of novel polypeptides, including the polypeptide designated PRO363, in an assay of stimulatory activity in the proliferation of rat utricular supporting cells (Assay #54, Example 116). This assay is used to find agents that are potent mitogens for inner ear supporting cells which are auditory hair cell progenitors. Such agents are useful for inducing the regeneration of auditory hair cells and treating hearing loss in mammals.

6. The assay is performed as follows. Rat UEC-4 utricular epithelial cells are aliquoted into 96 well plates with a density of 3000 cells/well in 200 ul of serum-containing medium at 33°C. The cells are cultured overnight and are then switched to serum-free medium at 37°C. Various dilutions of PRO polypeptides (or nothing for a control) are then added to the cultures and the cells are incubated for 24 hours. After the 24 hour incubation, 3H-thymidine (1 uCi/well) is added and the cells are then cultured for an additional 24 hours. The cultures are then washed to remove unincorporated radiolabel, the cells harvested and counts per minute (cpm) per well determined. Cpm of at least 30% or greater in the PRO polypeptide treated cultures as compared to the control cultures is considered a positive in the assay.

7. Copies of pages from an internal database showing the positive results for the PRO363 polypeptide (SEQ ID NO:59), identified by Pin number PIN665-1, in Assay #54 are attached to this declaration (with dates redacted) as **Exhibit B**. These experiments were performed and the results were obtained in the United States prior to May 19, 1999.

8. Exhibit B clearly shows that the polypeptide designated PRO363 was tested, and its ability to stimulate the proliferation of rat utricular supporting cells was determined prior to May 19, 1999. The column headed "mean" shows that addition of the PRO363 polypeptide to the rat utricular supporting cells resulted in an increase in proliferation of 37.1-51.9% as compared to control.

9. We hereby declare that all statements made herein of our own knowledge are true and that all statements made on information or belief are believed to be true, and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful statements may jeopardize the validity of the application or any patent issued thereon.

Luc Desnoyers, Ph.D.	Date 05/25/2006
Ellen Filvaroff, Ph.D.	Date
Wei-Qiang Gao, Ph.D.	Date
Audrey Goddard, Ph.D.	Date
Paul J. Godowski, Ph.D.	Date
Austin Gurney, Ph.D.	Date
William I. Wood, Ph.D.	Date

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